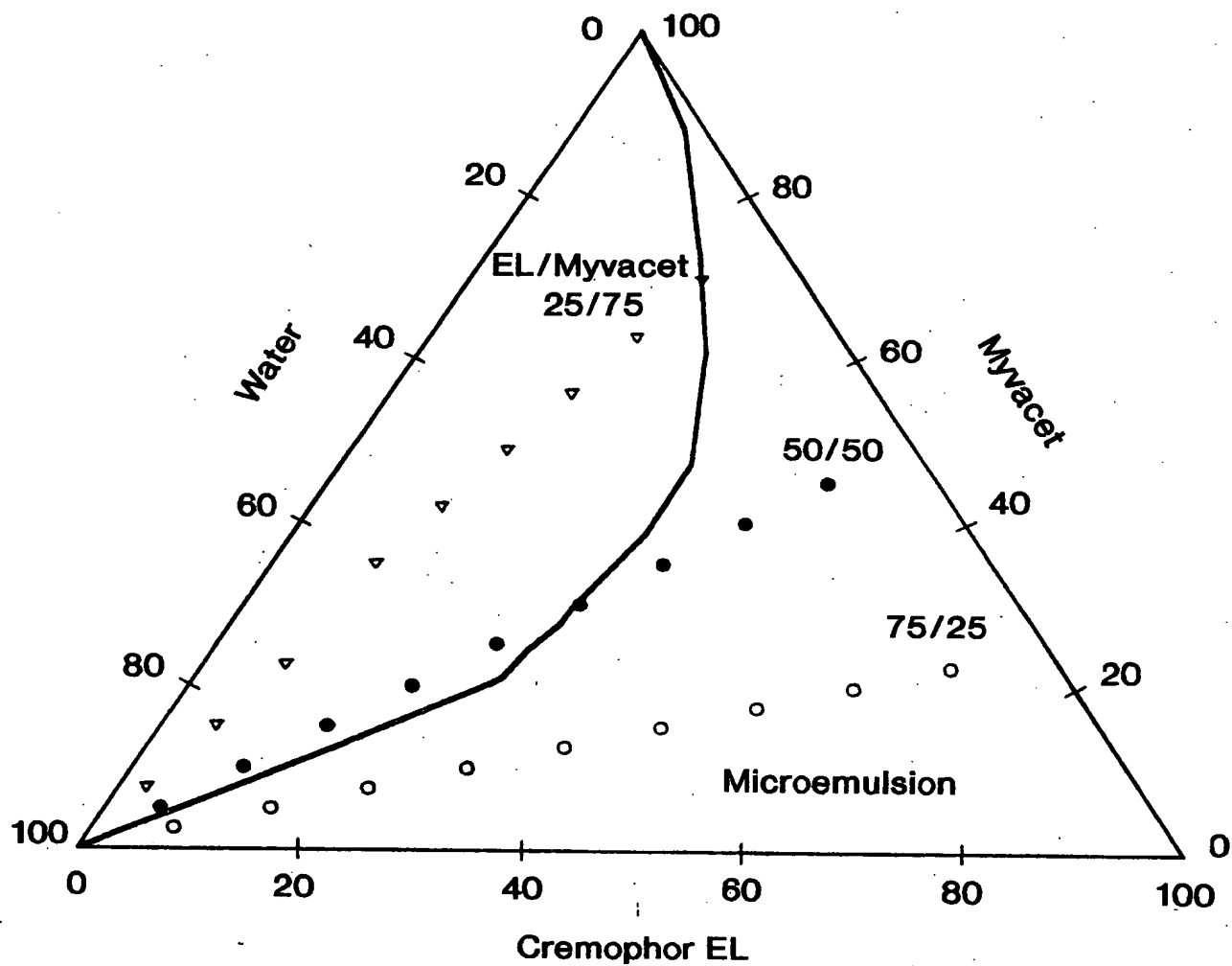


Figure 1 is a line graph showing the cumulative amount of 5-fluorouracil released (%) over time (hr) for three different S/O ratios: 100/0 (squares), 75/25 (filled squares), and 50/50 (diamonds). The release increases over time for all ratios, with the 100/0 ratio showing the highest release and the 50/50 ratio showing the lowest release. Error bars are included for each data point.

time (hr)	S/O:100/0 (%)	75/25 (%)	50/50 (%)
0	0	0	0
2	12	11	10
4	28	27	24
6	45	44	40
8	61	60	56
10	77	72	68
12	92	83	80
14	97	94	92
16	101	97	98
18	102	98	99

FIG. 6

000121-1610h260



Cremophor EL

FIG. 7

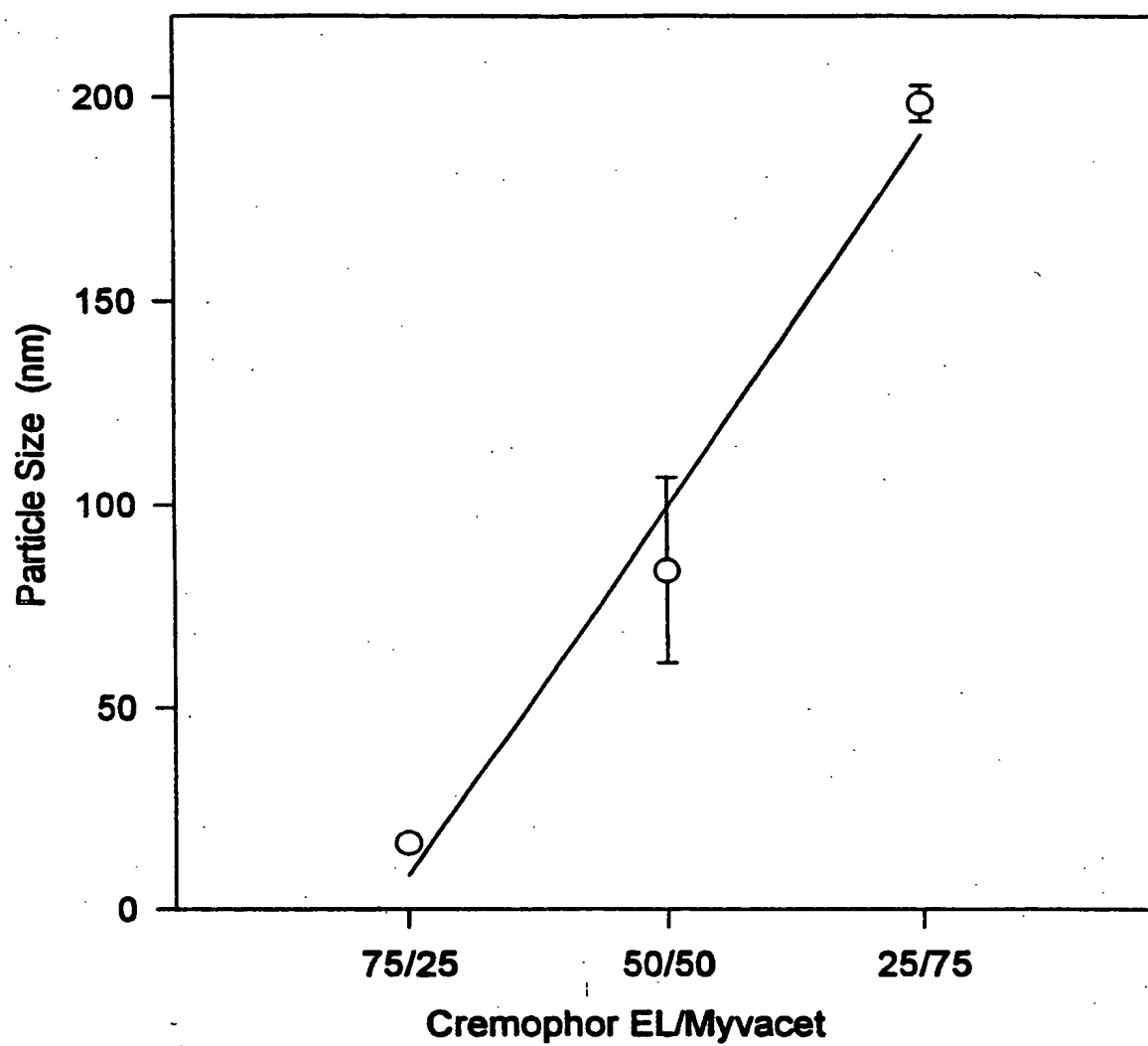
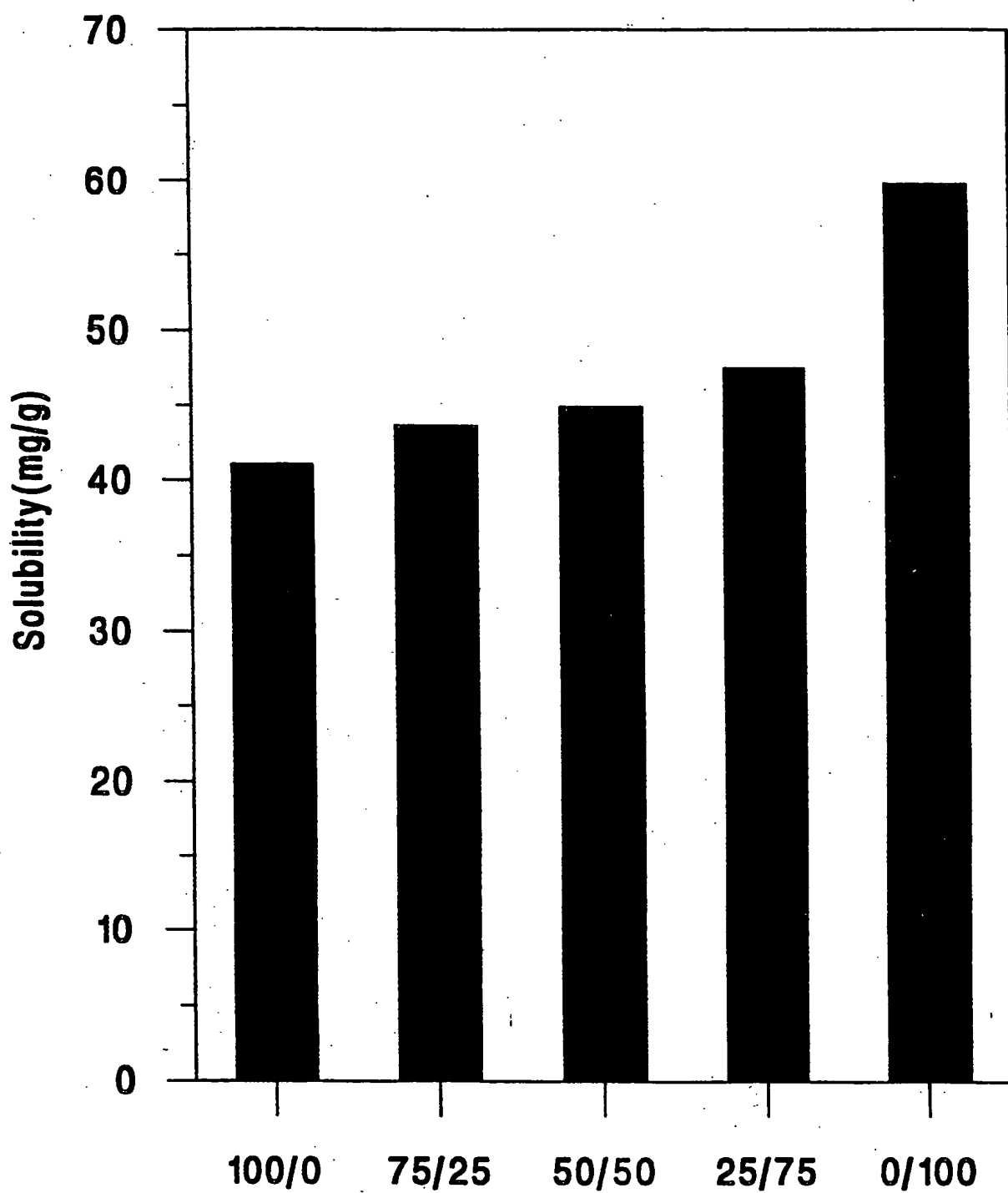


FIG. 8



Cremophor EL/Myvacet

FIG. 9

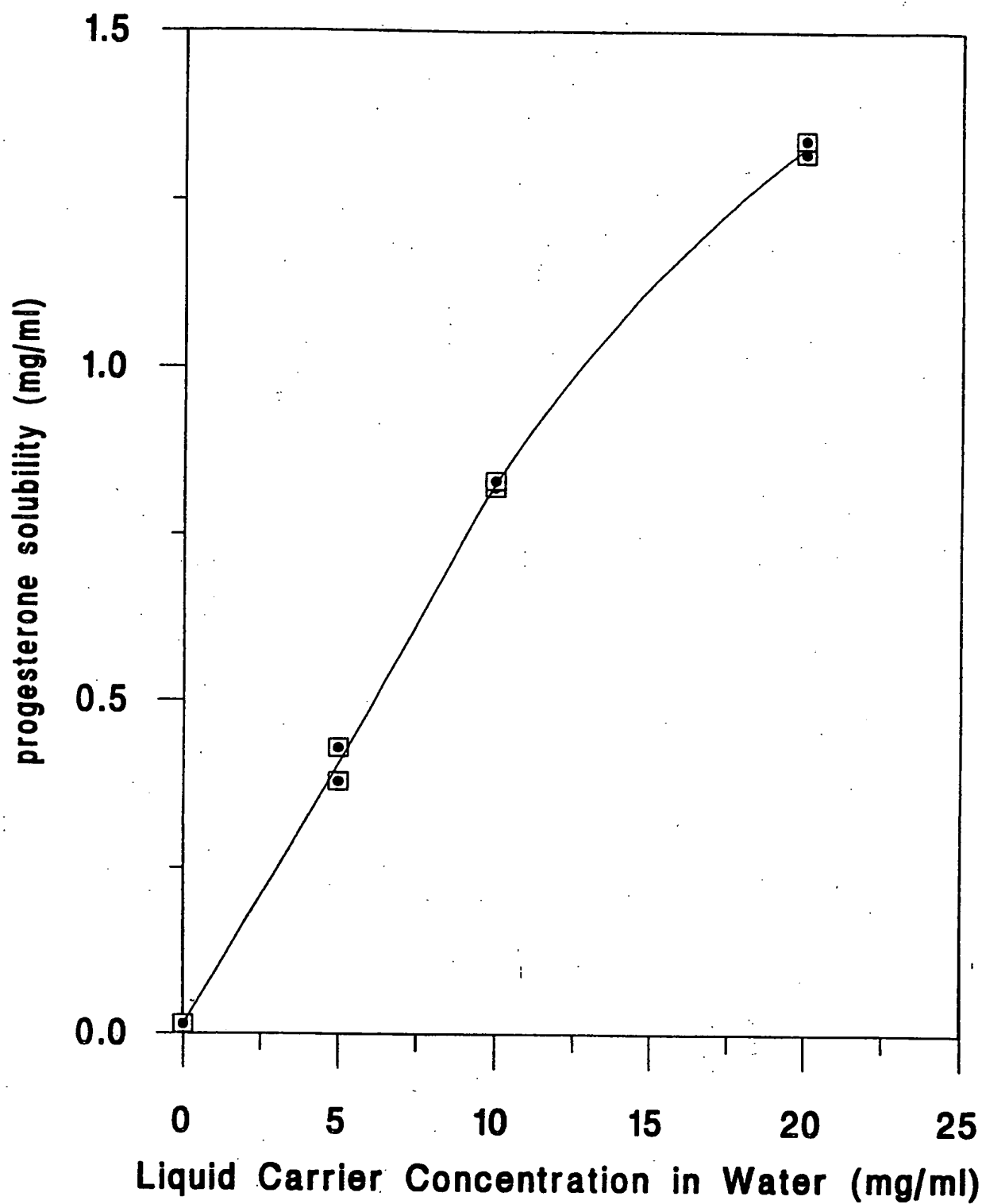


FIG. 10

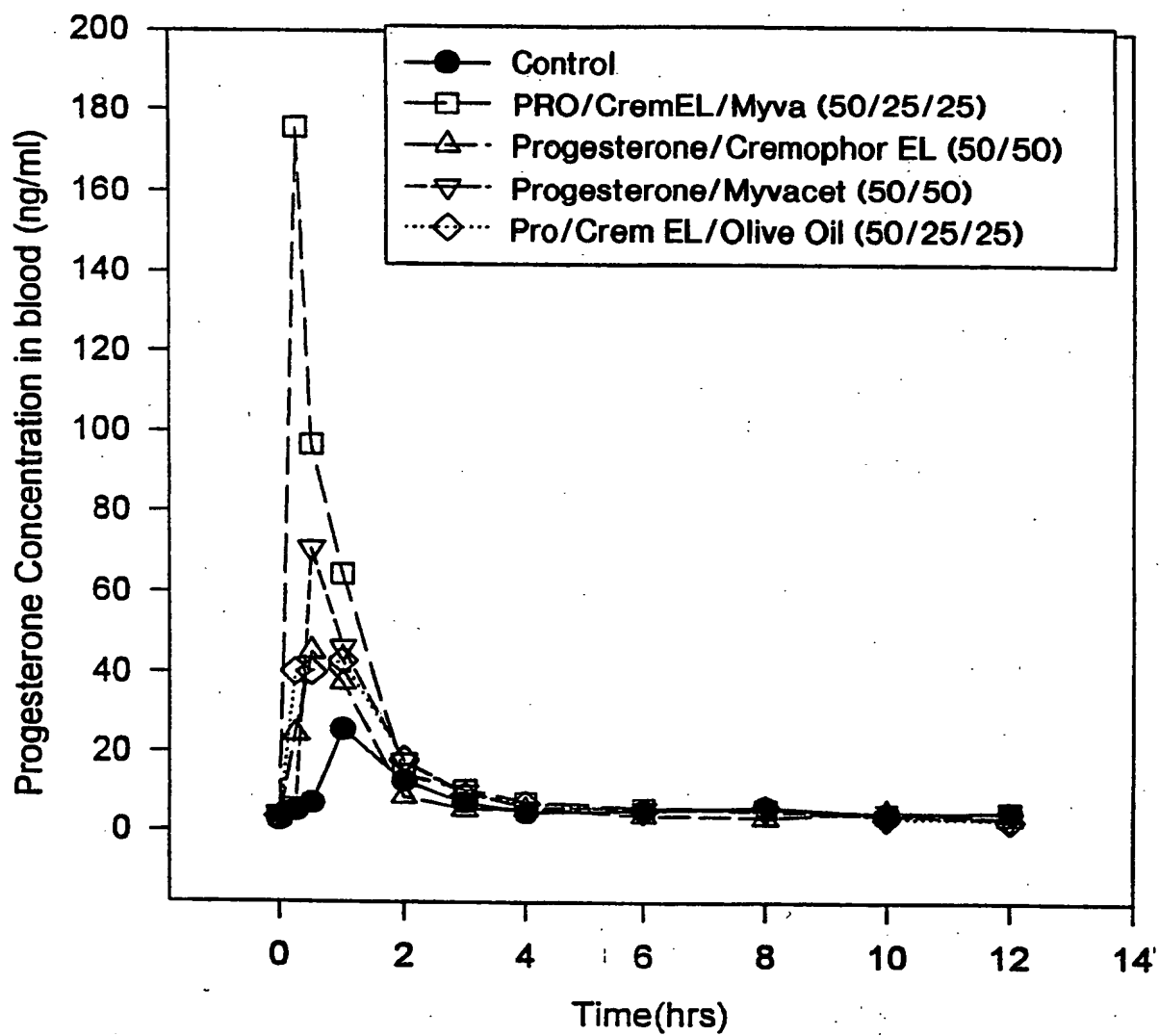


FIG. II

Figure 1: A line graph showing Progesterone Concentration in the Blood (ng/ml) versus Time (hrs) for three dogs (dog 1, dog 2, dog 3) at three different time points (0, 2, 4 hours). The concentration peaks sharply around 1-2 hours and then declines. Dog 3 shows the highest peak concentration, reaching approximately 5200 ng/ml at 1 hour. Dog 1 and Dog 2 show lower peaks, around 4800 ng/ml and 3400 ng/ml respectively at 1 hour. By 4 hours, the concentration for all dogs is significantly lower, around 200-300 ng/ml, and remains low through 12 hours.

Time (hrs)	in dog 1 (0h)	in dog 2 (0h)	in dog 3 (0h)	in dog 1 (2h)	in dog 2 (2h)	in dog 3 (2h)	in dog 1 (4h)	in dog 2 (4h)	in dog 3 (4h)
0	0	0	0	0	0	0	0	0	0
1	1800	3400	5200	0	700	600	0	0	0
2	4800	1300	1400	400	700	100	200	200	200
3	800	400	200	200	400	100	100	100	100
4	200	200	200	0	0	0	0	0	0
6	100	100	100	0	0	0	0	0	0
8	100	100	100	0	0	0	0	0	0
10	100	100	100	0	0	0	0	0	0
12	100	100	100	0	0	0	0	0	0

FIG. 13

**Pharmacokinetic Data for Oral Progesterone
Formulations Dosed to Dogs (40mg)**

Formulation #	T _{max} (h)			C _{max} (ng/ml)			AUC (ng/ml*h)	*Relative BA % Average (s.d)
	Dog 1	2	3	Dog 1	2	3		
1	1	1	1	38.4	13.9	24.4	104	100
2	0.25	0.50	0.25	252	90.8	248	226	232 (21)
3	0.50	0.25	0.50	53.4	57.7	33.7	109	130 (50)
4	0.5	1	1	174	57.1	30.4	167	176(108)
5	0.5	1	0.25	57.2	70.8	74.7	114	181(141)
			Avg			Avg (s.d).		
						25.6(12.3)	51	104
						197(92)	113	265
						48.3(12.8)	95	102
						87.2(76.4)	289	73
						67.5(9.1)	342	86

AUC is calculated by trapezoidal rule from time zero to the last blood sampling point (12h).

The relative bioavailability is the ratio of AUC for liquid formulations to that for laqueus drug-layer formulation.

Formulation Composition (wt%)

C mponents	Formulation #				
	1	2	3	4	5
Progesterone	60	4			4
Mannitol	21				
Ac-di-sol	10				
Myji 52-s	5				
HPMC E-5	3				
Mg stearate	1				
Cremophor EL		48	96		48
Myvacet 9-45		48		96	48
Olive oil					

**Pharmacokinetic Data for Emulsion Progesterone Formulation and
Nonemulsion Push-Pill Drug-Layer Formulation (300mg dose)**

F rmulation #	T _{max} (h)				C _{max} (ng/ml)				AUC (ng/ml*h)				Relative BA (%) Average (s.d)
	Dog 1	2	3	Avg	Dog 1	2	3	Avg (s.d).	Dog 1	2	3	Avg.(s.d)	
Nonemulsion	2	1	1	1.33	489	778	649	639(145)	1101	1715	898	1238(425)	100
Emulsion	1	1	1	1	4800	3420	5180	4467(926)	7715	4708	7418	6614(1657)	600 (289)

AUC is calculated by trapezoidal rule from time zero to the last blood sampling point (12h).

The relative bioavailability is the ratio of AUC for liquid formulations to that for MPA-22 drug-layer formulation.

Formulation Composition (wt%)

Components	Nonemulsion Drug-Layer	Emulsion Oral Formulation
Progesterone	60	50
Mannitol	21	
Ac-di-sol	10	
Myji 52-s	5	12.5
HPMC E-5	3	
Mg stearate	1	
Cremophor EL		25.0
Myvacet 9-45		12.5